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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,652	01/15/2002	Manuel L. Penichet	58086-223826	8739

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,652	PENICHET ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Penichet et al.

1. Applicant's amendment filed on 11/23/2005 is acknowledged. New claims 29 and 30 are added.

2. Claims 23-30 are pending and under examination.

3. The text of those sections of Title 35, U.S.Code not included in this action can be found in a prior office action.

Response to Arguments

4. The rejection of Claims 23-25, 26 and 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response states that the specification fully describes a variety of possible targeting moieties and receptors, for example, at page 6 in paragraph 32, wherein numerous receptor ligands and receptors are listed and one skill in the at would be able to make and test cytotoxic agents consisting of a targeting moiety and an avidin moiety, for example, insulin, epidermal growth factor, insulin like growth factor, erythropoietin, neurotrophic factor 3, etc. bound to, for example, avidin, streptavidin neutravidin, etc., as described in paragraph 33. The response states that the means for making and testing such compositions are known in the art, would not require undue experimentation.

Applicants' arguments have been carefully considered but are deemed not to be persuasive. Although the specification lists a number of receptors and their ligands on page 6, paragraph [0032], applicant does not appear to have reduced to practice any other targeting moieties and receptors except anti-transferring receptor antibody-avidin conjugate. The claims are drawn to a composition that binds to a genus of cell surface proteins or carbohydrates. A "cell surface protein or carbohydrate" encompasses any cell surface protein or any cell surface carbohydrate with the functional activity of binding to a ligand. A "targeting moiety or ligand" encompasses a variety of molecules with different structures and functions such as proteins (including antibodies), antisense nucleic acids, small peptides, organic compounds, inorganic ions, etc. The genus of molecules encompassed by the term "cell surface protein or carbohydrates", and "targeting moiety or ligand" recited in the claims is extensive. The number of the molecules encompassed by the genus is far more than those mentioned in the specification. The specification only discloses a composition comprising an antibody-avidin conjugate specific for a transferring receptor. Applicant does not appear to have reduced to practice the composition comprising any other targeting moiety or ligands (e.g. inorganic ions, cytokines) conjugated to avidin to any other cell surface proteins or carbohydrates. Therefore, the disclosure of a single species is insufficient to describe a highly variant genus and the artisan would not be able to recognize that applicant was in possession of the invention as now claimed.

5. The rejection of claims 23-28 under 35 U.S.C. 102(b) as being anticipated by Penichet et al (J. Immunol. 1999, 163: 4421-4426, see IDS) is maintained.

The response states that the antibody-avidin fusion protein with a biotinylated compound of Penichet is used for the purpose of delivering biotinylated compounds across the blood brain barrier, in contrast, the compositions of the present invention cause apoptosis and cell death. The response states that the presence of biotin is specifically excluded from the compositions of the present inventions. The response states that Penichet does not teach or suggest a composition comprising a cytotoxic agent consisting of a targeting moiety and an avidin moiety wherein said targeting moiety is capable of binding to one or more of said cell surface proteins or carbohydrates in combination with a pharmaceutically acceptable carrier. Furthermore, the response states that the present claims exclude any pharmaceutical compositions of Penichet et al. by the use of "consisting of ' in describing the cytotoxic compound.

Applicants' arguments have been carefully considered but are deemed not to be persuasive. Although Penichet et al. do not teach use of the composition for treating cells to induce apoptosis and/or inhibit cell proliferation, the claims are drawn to the product *per se* and the intended use of the composition for treating cells to induce apoptosis and/or inhibit cell proliferation is given no patentable weight. Moreover, Penichet et al. teach an antibody-avidin fusion protein specific for the transferring receptor (see abstract, and Figure 1). Penichet et al. teach that this fusion protein can be used for delivering biotinylated compounds, which again is just an intended use. Moreover, Penichet et al. teach a pharmaceutical carrier for study of pharmacokinetics

and brain delivery of the antibody-avidin fusion proteins (see page 4423, left column, 2nd paragraph, lines 4-8). Although the specification states that the presence of biotin is specifically excluded from the compositions of the present inventions, because claims use "a composition comprising:" on line 3 of claim 23, which is an open language, the claimed composition does not exclude any pharmaceutical compositions of Penichet. Therefore, Penichet et al. teach every limitation of the claims.

6. The rejection of claims 23-28 under 35 U.S.C. 102(a) as being anticipated by WO 01/07084 (see IDS) is maintained.

The response states that the fusion protein of WO 01/07084 is used in combination with additional agents to target biotin-linked compounds to cells. The compounds disclosed by WO 01/07084 undergo antibody-receptor-mediated endocytosis to deliver the attached cargo (biotin-linked compounds) to cells. The response states that the present application describes and claims cytotoxic agent consisting of a targeting moiety and an avidin moiety in combination with a pharmaceutical carrier. In contrast to the prior art, cells to which the claimed composition is administered undergo apoptosis and cell death. Furthermore, the presence of biotin is specifically excluded from the compositions of the invention (see, e.g. paragraph 11 of the specification).

Applicants' arguments have been carefully considered but are deemed not to be persuasive. Although WO 01/07084 does not teach use of the composition for treating cells to induce apoptosis and/or inhibit cell proliferation, the claims are drawn to the

product *per se* and the intended use of the composition for treating cells to induce apoptosis and/or inhibit cell proliferation is given no patentable weight. Moreover, WO 01/07084 teaches the claimed product comprising a first segment and a second segment: the first segment comprising a variable region of an antibody that recognizes transferring receptor (claims 6-7) and further comprises at least one domain of a constant region of an antibody; and the second segment comprising a protein domain selected from the group consisting of avidin, an avidin mutein, a chemically modified avidin derivative, streptavidin, etc (Claim 1). WO 01/07084 further teaches a pharmaceutical carrier for study of pharmacokinetics and brain delivery of an antibody-avidin fusion protein (see page 29, second paragraph, lines 20-25). Although the instant specification states that the presence of biotin is specifically excluded from the compositions of the present inventions, because claims use "a composition comprising:" on line 3 of claim 23, which is an open language, the claimed composition does not exclude any pharmaceutical compositions of WO 01/07084. Therefore, WO 01/07084 teaches every limitation of the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

7. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The newly presented claim 29 contains the limitation that the targeting moiety is a chemical conjugate. The support pointed to by applicant for this new claim on paragraph 35 and 36 is not found. Moreover, there is no adequate support for the claimed chemical conjugate in the specification. Therefore, the newly presented claim 29 introduces new matter into the specification as originally filed.

Claim Rejections - 35 USC § 102

8. Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Penichet et al (J. Immunol. 1999, 163: 4421-4426, see IDS).

Claim 30 is a composition of claim 23, wherein said avidin moiety is selected from the group consisting of avidin, streptavidin, neutra-avidin, lite-avidin, and neutra-lite avidin.

The teachings of Penichet are set forth above as they apply to claims 23-38(see paragraph 5 and the previous office action).

Because Penichet teaches the avidin moiety is avidin, the claim limitation is met.

9. Claims 30 is under 35 U.S.C. 102(a) as being anticipated by WO 01/07084 (see IDS).

Claim 30 and its interpretation are set forth above (see paragraph 8).

The teachings of WO 01/07084 are set forth above as they apply to claims 23-28 (see paragraph 6 and previous office action).

Because WO 01/07034 teaches the avidin moiety is avidin, an avidin mutein, a chemically modified avidin derivative, or streptavidin, etc, the claim limitation is met.

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit: 1643
Dec. 23, 2005

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER